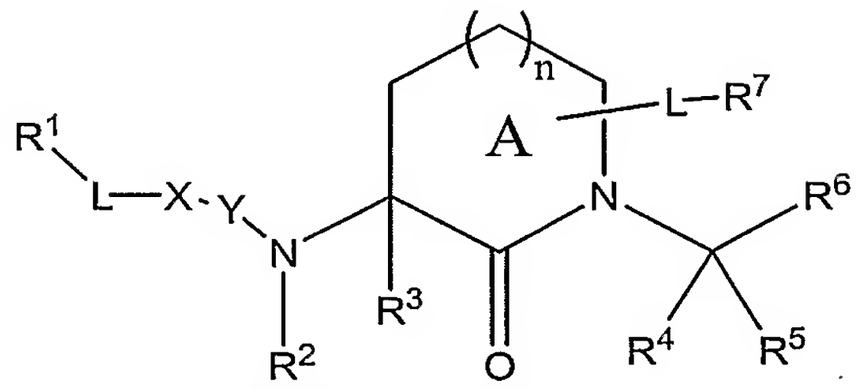
We claim:

1. A compound having a structure of formula



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from H, alkyl, alkoxy, alkenyl, alkynyl, amino, alkylamino, acylamino, cyano, sulfonylamino, acyloxy, aryl, cycloalkyl, heterocyclyl, heteroaryl, and a polypeptide chain of 1 to 8 amino acid residues;

R^2 and R^3 are independently selected from H, lower alkyl, cycloalkyl, and aralkyl; or R^2 and R^3 together with the atoms to which they are attached, form a 4- to 6-membered heterocyclic ring;

R^4 and R^5 are independently selected from H, halogen, and alkyl, or R^4 and R^5, together with the carbon to which they are attached, form a 3- to 6-membered carbocyclic or heterocyclic ring;

R^6 is a functional group that reacts with an active site residue of a targeted protease to form a covalent adduct;

R^7 is absent or is one or more substituents on ring A, each of which is independently selected from H, lower alkyl, lower alkenyl, lower alkynyl, hydroxyl, oxo, ether, thioether, halogen, carbonyl, thiocarbonyl, amino, amido, cyano, nitro, azido, alkylamino, acylamino, aminoacyl, cyano, sulfate, sulfonate, sulfonyl, sulfonylamino, aminosulfonyl, alkoxycarbonyl, acyloxy, aryl, cycloalkyl, heterocyclyl, heteroaryl, and a polypeptide chain of 1 to 8 amino acid residues;

R^8 is selected from H, aryl, alkyl, aralkyl, cycloalkyl, heterocyclyl, heteroaryl, heteroaralkyl, and a polypeptide chain of 1 to 8 amino acid residues;

L is absent or is selected from alkyl, alkenyl, alkynyl, $-(CH_2)_mO(CH_2)_m-$, $-(CH_2)_mNR^2(CH_2)_m-$, and $-(CH_2)_mS(CH_2)_m-$;

X is absent or is selected from $-N(R^8)-$, -O-, and –S-;

Y is absent or is selected from -C(=O)-, -C(=S)-, and $-SO_2-$;

m is, independently for each occurrence, an integer from 0 to 10; and

n is an integer from 0 to 3.

2. A compound of claim 1, wherein R^6 is selected from cyano, boronic acid, $-SO_2Z^1$, $-P(=O)Z^1$, $-P(=R^9)R^{10}R^{11}$, $-C(=NH)NH_2$, $-CH=NR^{12}$, and $-C(=O)-R^{12}$ wherein:

R^9 is O or S;

R^{10} is selected from N_3, SH_2, NH_2, NO_2, and OLR^{13}, and

R^{11} is selected from lower alkyl, amino, OLR^{13}, or a pharmaceutically acceptable salt thereof, or

R^{10} and R^{11}, together with the phosphorus to which they are attached, form a 5- to 8-membered heterocyclic ring;

R^{12} is selected from H, alkyl, alkenyl, alkynyl, $-(CH_2)_p-R^{13}$, $-(CH_2)_q-OH$, $-(CH_2)_q-O$-alkyl, $-(CH_2)_q-O$-alkenyl, $-(CH_2)_q-O$-alkynyl, $-(CH_2)_q-O-(CH_2)_p-R^{13}$, $-(CH_2)_q-SH$, $-(CH_2)_q-S$-alkyl, $-(CH_2)_q-S$-alkenyl, $-(CH_2)_q-S$-alkynyl, $-(CH_2)_q-S-(CH_2)_p-R^{13}$, $-C(O)NH_2$, $-C(O)OR^{14}$, and $C(Z^1)(Z^2)(Z^3)$;

R^{13} is selected from H, alkyl, alkenyl, aryl, cycloalkyl, cycloalkenyl, and heterocyclyl;

R^{14} is selected from H, alkyl, alkenyl, and LR^{13};

Z^1 is a halogen;

Z^2 and Z^3 are independently selected from H or halogen;

p is, independently for each occurrence, an integer from 0 to 8; and

q is, independently for each occurrence, an integer from 1 to 8.

3. A compound of claim 1, wherein a R^6 is a group of formula $-B(Y^1)(Y^2)$, wherein Y^1 and Y^2 are independently OH or a group that is hydrolysable to OH, or together with the boron atom to which they are attached form a 5- to 8-membered ring that is hydrolysable to a boronic acid.

4. A compound of claim 1, wherein the compound is a protease inhibitor.

5. The inhibitor of claim 5, wherein the protease inhibitor inhibits dipeptidyl peptidase IV (DPIV) with a K_i of 50 nm or less.

6. A compound of claim 1 that is orally active.

7. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 1, or a pharmaceutically acceptable salt or prodrug thereof.

8. The use of a compound of claim 1 in the manufacture of a medicament for inhibiting a post-proline-cleaving enzyme.

9. The use of claim 9, wherein the compound increases plasma concentrations of a peptide hormone selected from glucagon-like peptide, NPY, PPY, secretin, GLP-1, GLP-2, and GIP.

10. The use of a compound of claim 1 in the manufacture of a medicament for regulating glucose metabolism.

11. The use of claim 11, for regulating glucose metabolism of a patient suffering from Type II diabetes, insulin resistance, glucose intolerance, hyperglycemia, hypoglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.

12. A method for inhibiting the proteolytic activity of a post-proline-cleaving enzyme, comprising contacting the enzyme with a compound of claim 1.

13. A packaged pharmaceutical comprising a preparation of a compound of claim 1 and instructions describing the use of the preparation for inhibiting a post-proline cleaving enzyme.

14. A packaged pharmaceutical comprising a preparation a compound of claim 1 and instructions describing the use of the preparation for regulating glucose metabolism.

15. The packaged pharmaceutical of claim 15, wherein the compound is co-formulated with or co-packaged with insulin, an insulinotropic agent or both.

16. The packaged pharmaceutical of claim 15, wherein the compound is co-formulated with or co-packaged with one or more of an M1 receptor antagonist, a prolactin inhibitor, an agent acting on the ATP-dependent potassium channel of β-cells, metformin, and a glucosidase inhibitor.